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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/509,695 | 09/30/2004 | Jacques Froissant | SSL0065 | 2175 |

5487 7590 12/08/2006

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EXAMINER

HABTE, KAHSAY

ART UNIT PAPER NUMBER

1624

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/509,695

Applicant(s)

FROISSANT ET AL.

Examiner

Kahsay Habte

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 15-56 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15 and 26-56 is/are rejected.
- 7) ☒ Claim(s) 1-10, 13 and 16-25 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>9/30/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-13 and 15-56 are pending in this application.

Election/Restriction

2. Applicant's election with traverse of Group I, Claims 1-10 and 13-56 filed 11/14/2006 is acknowledged. The traversal is on the ground(s) that the (1) there is no undue burden to the Examiner to search for all of the claims as they are believed to be in same classification, and (2) there was no lack of unity of invention imposed on the corresponding PCT application. The examiner disagrees with applicants. The special technical feature of Group I is pyridazno[4,5-b]indole ring that is different from the special technical feature of Group II i.e. indole ring. Group I is drawn to tricyclic ring and classified in class 544/234 that is different from the classification of the indole ring. Indoles are classified in class 548. Coexamination of the additional group would require search of subclasses unnecessary for the examination of the elected claims. The search for the invention of Group II would include search in class 548 and also separate search in STN chemical search and EAST/WEST databases. Therefore, coexamination of the additional invention would require a serious additional burden of search. In regard to the argument that there was no lack of unity of invention imposed on the corresponding PCT application, the examiner disagrees with this argument. This restriction requirement is not bound by the restriction requirement in the corresponding PCT application.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement, filed on 9/30/2004 has been acknowledged. Please refer to Applicant's copies of the 1449 submitted herewith.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In claims 41-56, it is recited a method of treatment of pathologies in which peripheral benzo-diazepine receptors are involved, but the specification is not enabled for such a scope.

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the

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art, and (8) the breadth of the claims.” In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The instant claims recite “A method for the treatment of pathologies in which the peripheral benzo-diazepine receptors are involved” and the specification on page 40 provides that composition of compounds of claim 1 can be used for the treatment or prevention of various types of peripheral neuropathies such as neurodegenerative diseases, central nervous system disorders including Alzheimer’s disease and Parkinson’s Disease, stroke auto immune diseases, etc. some of which have been proven to be extremely difficult to treat. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 1 51 USPQ 724 regarding sufficiency of disclosure for a Markush group.

The scope of the claims is not adequately enabled solely based on the involvement of peripheral benzo-diazepine receptors. The specification does not disclose biological data with respect to involvement of peripheral benzo-diazepine receptors. There is nothing in the disclosure regarding how this data correlates to the treatment of all the disorders embraced the instant claims. The disorders encompassed by the instant claims include the prevention and the treatment of various diseases such as neurodegenerative diseases, central nervous system disorders including Alzheimer’s

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disease and Parkinson's Disease, stroke auto immune diseases, etc. that are hard to treat.

According to a review article by Lacapere et al. Steroids 68 (2003) 569-585, there is no mention for the treatment of many of the diseases disclosed at pages 25-26 of the specification. In addition, at page 580 (first column), the authors indicate that "Several questions remain unanswered to understand the PBR molecular mechanism leading to the transfer of cholesterol from cytosol to the inner mitochondrial membrane." This indicates that the study to understand the basic molecular mechanism of peripheral benzo-diazepine receptors is at its early stage.

Thus, factors such as 'sufficient working examples', 'the level of skill in the art' and 'predictability', etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 26-40 and 41-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a. Claims 15 and 26-40 are rejected because the phrase "A pharmaceutical composition comprising at least one compound of formula (I) according to claim 2.....the solvate of this compound, optionally combined with at least one pharmaceutically acceptable excipient" is not clear. Note that the pharmaceutical composition would lack a pharmaceutically acceptable carrier or excipient if it is not combined with at least one pharmaceutically acceptable excipient or carrier. The term "optionally" should be deleted from the phrase, since a carrier or excipient is always required for a pharmaceutical composition.

b. In claims 41-56, it is recited "A method for the treatment of pathologies in which the peripheral benzo-diazepine receptors are involved". The scope of claims 41-56 is unknown. Which pathologies are these? Determining whether a given disease responds or does not respond to such mediator will surely involve undue experimentation. Suppose that a given inhibitor X when administered to a patient with Disease D does not obtain a response. Does one then conclude that Disease D does not fall within this claim? Keep in mind that:

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A. It may be that the next patient will respond. It is quite common for pharmaceuticals to work only with some people, not all. Thus, how many need to be tested?

B. It may be that the wrong dosage or dosage regimen was employed. It is quite common for pharmaceuticals to work at one dosage, but not at another which is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? Thus, how many dosages and dosage regimens must be tried before one is certain that this pharmaceutical won't affect Disease D?

C. It may be that X simply isn't potent enough for Disease D, but that another inhibitor Y is potent enough, so that D really does fall within the claim. Thus, how many different mediators must be tried before one concludes that D doesn't fall within the claim?

D. Conversely, if D responds to Y but not to X, can one really conclude that D falls within the claim? It may be that the X result is giving the accurate answer, and that the success of Y arises from some other unknown property which Y is capable of. Thus, when mixed results are obtained, how many more pharmaceuticals need be tested?

E. Finally, suppose that X really will work, but only when combined with Z. There are for example, agents in the antiviral and anticancer technology which are not themselves effective, but the disease will respond when the agents are combined with something else.

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F. In addition, literally speaking, any disorder can be treated with any drug, although the treatment might not be successful. Assuming that "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000?

As a result, determining the true scope of the claim will involve extensive and potentially open-ended research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

c. In claims 41-56, the phrase "to a patient in need of such treatment" is not clear. Who is in need thereof and who is not?

Claim Objections

6. Claims 1, 7-10 and 13 (and claims dependent thereon) are objected to because of the following informalities: the recitation of "general formula" is objected because a formula should be specific. It is recommended that applicants delete the term "general" from claims 1, 7-10 and 13 to overcome this objection.

Allowable Subject Matter

7. Claims 2-6 and 16-25 would be allowable if applicants overcome the claim objection raised above. Note that the closest prior art is Burnier et al. U. S. Pat. No. 7,109,194. The instant application is different from Burnier '194, since it requires an

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additional -CH₂- linker to the CO-NR₂R₃ that is attached at 3-position of the tricyclic ring.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte whose telephone number is (571)-272-0667. The examiner can normally be reached on M-F (9.00- 5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kahsay Habte
Primary Examiner
Art Unit 1624

KH
December 6, 2006